The power to...

Balance inflammation

On one hand, our immune system keeps us safe from infection; on the other, chronic inflammation is a core part of nearly everything that ails us, from lower back pain to cancer to Alzheimer’s disease.

The challenge

The immune system is a powerful biological force—a liquid organ that permeates our bodies, infiltrating all tissues and organs. Diverse immune cells are constantly on patrol, hunting for bacteria, viruses, tumors and cellular garbage. They keep us safe in a hostile world.

But as important as the immune system is for protecting us from pathogens and other dangers, it can be a double-edged sword. Immune cells can destroy cancer or help it thrive; they can defeat pathogens or generate a dangerous autoimmune response. Chronic inflammation is the root of many diseases, including cancer, heart disease, type 2 diabetes, obesity and neurodegenerative diseases such as Alzheimer’s.

COVID-19 provides an example: People who are immunocompromised, meaning their immune systems are weakened by age or disease, are especially vulnerable to the coronavirus—it invades cells and replicates without much resistance. People with underlying inflammatory conditions, such as age-related inflammation, hypertension and type 2 diabetes, are also at higher risk for severe COVID-19.

Yet many people with robust immune systems also experience severe COVID-19. That’s often not due to the coronavirus itself but to a “cytokine storm,” a phenomenon in which the patient’s own immune system overreacts, sending a flood of cells to wreak havoc in the lungs. Many of the infection’s long-term effects—often called “Long COVID”—are also thought to result from damage by one’s own immune response.

For many disease states, a central question remains: What tips immune function from helpful to harmful?

The Salk approach

At Salk, researchers in the NOMIS Center for Immunobiology and Microbial Pathogenesis are deciphering the complex interplay between our genes, molecules, cells and microbiomes—the unique collections of bacteria and viruses that live in harmony with us—to better understand how we sustain health and develop tolerance to disease.

And like the immune system itself, NOMIS researchers are all around the Institute, embedded in virtually every discipline to probe how our immune system influences cancer, brain health, genome integrity, aging and metabolism.

See the Salk approach at work:

Finding balance

Launched in 2008, the NOMIS Center illuminates the mechanisms associated with infections and inflammation—but that’s just the start.

Immune balance in cancer. Because the immune system is everywhere, it can be an ideal tool to fight cancer. Unfortunately, cancer figures this out as the tumor progresses and has developed effective countermeasures. Tumors often send false signals to fool immune cells into thinking they are normal tissue.

Even more worrisome, cancer cells can convince immune cells to switch allegiance and become part of the tumor’s support system. We are making tremendous headway in understanding these tumor signaling mechanisms, but there’s a lot more we need to know.

After an infection or vaccination, our immune systems develop memory T cells to remember and protect against future infections by the same pathogen. But memory T cells can also protect against cancer.

Pioneering work by Professor Susan Kaech, who directs the NOMIS Center, led to the discovery of the pathways that control memory T cell development. Now Kaech and colleagues are directing memory T cells to attack cancer and exploring how different immune and nonimmune cells communicate. Understanding these various inputs could offer new tools to unleash the immune system—in a controlled way—to attack cancer.

Kaech is also interested in how tumors use metabolism to protect themselves. Like people, immune cells don’t perform well when they are hungry. In a recent study, the Kaech lab showed that tumors can flood their surroundings with oxidized fat molecules. This “bad” fat can make T cells lethargic and less likely to attack the tumor.
Immune balance in infectious diseases. Society is in an arms race with pathogens. One major way we defend ourselves is by developing long-term memory T cells, but another way is to develop tolerance.

It was a long-standing belief that the human body needed to kill an invading pathogen in order to survive. But Professor Janelle Ayres discovered the body’s cooperative defense system, a collection of mechanisms that prevent damage to the body during infection. The system changes the behavior of pathogens so they don’t cause disease—turning foes into friends.

This naturally occurring tolerance mechanism can teach us how to promote health without killing pathogens too. By leveraging our own cooperative defense system, we might be able to give a patient’s immune system the opportunity to take care of the pathogen on its own. This therapeutic approach would likely have fewer side effects, and because it doesn’t directly kill microbes (the way antibiotics do), they are less likely to evolve resistance.

Immune balance in neurodegeneration. The immune system doesn’t roam quite as freely in the brain, thanks to specialized protective barriers. Instead, the brain has some of its own unique immune components. Despite these differences, though, chronic inflammation is also increasingly appreciated as a major contributor to neurodegenerative diseases, such as Alzheimer’s.

Salk scientists are unraveling inflammation’s role in the brain and are looking for ways to tip the balance to preserve resilience. One example is Professor Greg Lemke, who studies TAM receptors. Found on immune cells called macrophages, as well as other cells, these receptors shut down the immune response after it has cleared out the invader. But dysfunctional TAM signaling can lead to adverse consequences for microglia, the brain’s macrophages. Without TAM-directed signals, microglia stop clearing away dead cells, which contributes to neurodegenerative diseases.

Why Salk
The Salk Institute is the house that immunology built. Jonas Salk’s groundbreaking work on the first polio vaccine propelled him to national attention and helped create a world-class research institute. Even as the Institute has branched out into cancer, neurology and other fields, we always remember our roots.

Some of our past immunobiology breakthroughs include the following:

1968 – Renato Dulbecco published his discovery that viruses can cause cancer by inserting genes into the chromosomes of infected cells. He was awarded the Nobel Prize for the discovery in 1975.

1987 – Wylie Vale and colleagues discovered the link between the immune system and the brain.

Immunology studies are now at a scientific crossroad, providing incredible opportunities to maximize collaboration and discovery. Understanding the immune response and the pathways that lead to chronic inflammation will be essential to treating virtually any condition, from heart disease to Alzheimer’s.

The work being done at the NOMIS Center for Immunobiology and Microbial Pathogenesis is central to how we understand biology and our efforts to develop more advanced treatments.

Why now
In 2019 the Salk Institute launched the Campaign for Discovery—a seven-year, $750 million effort to accelerate Salk’s critical research.

The Campaign is focused on driving discoveries in six Centers of Excellence: Cancer Center, Center for Healthy Aging, Center for Plant Biology, Center for Neuroscience, NOMIS Center for Immunobiology and Microbial Pathogenesis, and Crick-Jacobs Center for Theoretical and Computational Biology.

To continue to lead the field in these areas, Salk is recruiting new faculty and other experts, investing in new technologies, and creating new collaborative spaces, including construction of the Joan and Irwin Jacobs Science and Technology Center.

As it has always been at Salk, there will be no barriers between disciplines. New ideas from multiple areas can mix and flourish, generating the most innovative, multipronged approaches to decoding inflammation and its role in health and disease.

Join us
Science is a collaborative pursuit, and we invite you to join us in accelerating life-changing discoveries: www.salk.edu/campaign.